LEBANON VAMC PHARMACY

Pharmacotherapy Update

Volume 5, Issue 2 Winter 2013- 2014

A Note from the Editors

While we've already said hello to 2014, it would be a shame if we didn't touch on the climactic end to 2013. During the last quarter of 2013, not one, but two major guideline updates came to the area of primary care. November saw the release of ATP IV…no, wait…it was actually ACC/AHA that released the new cholesterol guidelines.

Then, right before the end of the year, new hypertension guidelines were delivered to us like an early Christmas present. Unfortunately, for those of us that are a fan of beta-blockers, this was more like a stocking filled with coal.

So as we wait for direction from the national office on the new guidelines, let's take a moment and officially say goodbye to 2013 (and wait in anticipation for the new diabetes updates scheduled to come in 2014).

This edition of the newsletter bears many gifts. Steve Gruver, first year resident and all-around great guy, takes us to the Drug Information Corner for a look at what to do with psychiatric medications in the inpatient setting. In our Literature Review section, Christina Inteso, a PharmD candidate in her final year at Wilkes University, breaks down a trial investigating if applying intensive lifestyle modifications in diabetic patients decreases cardiovascular morbidity and mortality. And our New Drug Alert section brings information regarding an inhaler for the treatment of COPD that was approved by the FDA just before the end of 2013.

The latest news from the FDA is also covered in this edition. Recent generic releases, as well as medications anticipated to go generic, are presented. Noteworthy updates from the FDA's MedWatch program are also reported. Big news also came out from the VA National Formulary- find out all about it on page 5.

We wrap things up with a spotlight feature on one member of the pharmacy staff here at Lebanon and look at the field of pharmacy through the lens of pop culture.

Enjoy.

Tawes Harper, PharmD
Dina Hunsinger-Norris, PharmD, BCPS

New Drug Alert: ANORO™ ELLIPTA™ for COPD

Chronic Obstructive Pulmonary Disease (COPD) is the third leading cause of death in the United States, behind only heart disease and cancer. Most recent estimates from 2011 state that up to 12.7 million U.S. adults have COPD and 10.1 million have a diagnosis of chronic bronchitis, with persons aged 65 years or older having the highest rate at 64.2 per 1,000 persons for the latter.[1] Reducing COPD readmission rates has become an important focus at hospitals all across the country, supported by data collected by the Centers for Medicare & Medicaid Services (CMS) showing national 30 day readmission rates for COPD patients being greater than 20% each year over the last decade.[2]

Long-term medication treatment options vary based off of severity classification outlined in the GOLD guidelines. The mainstay of drug therapy includes short or long-acting $beta_2$-agonists, short or long-acting anticholinergics and corticosteroids, with different classes being used in combination for more severe disease.[3]

Last year, the FDA granted approval to two

Continued on Page 7

Inside this issue:

Drug Information Corner

Stephen N. Gruver, PharmD

To Continue or Discontinue? Psychiatric Meds

According to 2002-2003 data from the Substance Abuse and Mental Health Services Administration (SAMHSA), approximately 1.2 million male veterans were identified as living with serious mental illness.[1] Additionally, many of these veterans are also battling chronic and acute conditions which cause them to arrive at Veteran Affairs Medical Center (VAMC) emergency rooms around the country. Consequently, a common, challenging question arises when admitting these patients: how should their psychoactive medications be managed? The answer is highly dependent on each patient and requires clinical experience and judgment.

Prior to arriving at the decision to either continue or discontinue, some general tips can be utilized to help evaluate the situation. Evaluate if the psychoactive medication is affecting the patient's primary medical issue through any of the following mechanisms:

- Has the patient been compliant?
- Has the veteran had any recent medication changes?
- Any drug interactions?
- What are the adverse drug effects?

The answers to these questions can assist in the decision making process. For instance, if the patient has not been compliant on the particular medication for an extended period of time, not initiating the medication as an inpatient may be a straight forward option to avoid possible side-effects. Conversely, recent abrupt discontinuation could be the source of the patient's chief complaint.[2]

Although discontinuing psychiatric medications can seem to be a knee-jerk reaction, the consequences should be considered. In schizophrenic patients, relapses can be more severe than the original illness and even restarting the medication may not return the patient to their prior baseline.[2] Temporarily holding an agent may create issues as well. Cessation of lithium can lead to mania in bipolar patients in as soon as four days.[2] Additionally, withdrawal can be seen with selective serotonin reuptake inhibitor (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs). Known as serotonin discontinuation syndrome, it can also be referred to as FINISH syndrome due to its symptoms [Table 1].[4] The incidence increases with chronic use of a SSRI or SNRI and is more common in agents with shorter half-lives [Table 2].[5] In order to avoid this complication, it is recommended to taper over 4 weeks. Reducing the starting dose by 25% every 4-6 weeks may be necessary for paroxetine and venlafaxine due to short half-lives.[2,4]

TABLE 1: **FINISH Syndrome**

Flu-like illness
Insomnia
Nausea
Imbalance
Sensory disturbances
Hyperarousal

Benzodiazepines are another drug class with known withdrawal syndrome. The onset is anywhere from 2-10 days after cessation. Symptoms mirror alcohol withdrawal including tremor, insomnia, anxiety, seizures and delirium.[2] Tapering will lessen the likelihood of these symptoms and can be performed directly or indirectly. A direct taper would involve weekly decreases of the current benzodiazepine over a month or so, depending on duration of use and dose. Indirect tapering involves first switching the patient to an equipotent dose of diazepam, since it has a longer half-life and less likely to cause serious symptoms, and then taper.[4] In general, if stopping a psychoactive medication is required, tapering the dose is recommended to prevent withdrawal or relapse.

On the other hand, the decision to continue a psychoactive medication comes with its share of issues as well. One of particular concern is drug interactions. Serotonin syndrome is a result of the concomitant administration of two serotonin-targeted agents or an SSRI and an inhibitor of cytochrome P450 (primarily CYP 2D6). If suspected, monitor for acute mental status changes, autonomic instability and neuromuscular hyperactivity. Signs usually appear within 24 hours.[2,6] Another dangerous interaction occurs when two monoamine oxidase inhibitors (MAOIs) are taken together resulting in a hypertensive crisis. This can also happen between MAOIs and sympathomimetic agents or linezolid. To prevent this from occurring, an MAOI must be discontinued 14 days prior to initiating any of the aforementioned

Continued on Page 5

Literature Review

Christina Inteso, PharmD Candidate 2014
Wilkes University

Cardiovascular Effects of Intensive Lifestyle Intervention in Type 2 Diabetes

The Look AHEAD Research Group. *N Engl J Med.* 2013 Jul 11;369(2):145-54.

Background: Healthcare professionals are always suggesting lifestyle modifications such as dietary changes and increased physical activity to their patients. Some benefits have been shown with these modifications in certain disease states, but it is uncertain how these changes affect type 2 diabetics in the long run. Short-term studies in diabetics have shown improvements in glycemic control, cardiovascular disease risk factors, quality of life, and other obesity-related coexisting illnesses. Up to this point, no long-term studies have examined the effects of sustained weight loss in diabetics. A meta-analysis of cohort studies concluded that moderate intentional weight loss was associated with reduced mortality among patients who were classified as "unhealthy", a group which included diabetics. The Swedish Obese Subjects (SOS) study followed type 2 diabetics who underwent bariatric surgery for 13.3 years and found reduced rates of cardiovascular (CV) events. The study was not randomized and does not apply to all patients.

Objectives: Does intensive lifestyle modification decrease CV morbidity and mortality?

Intervention:

Intensive lifestyle intervention
- Goal was to achieve and maintain weight loss of at least 7% by focusing on decreased caloric intake and increased physical activity
  - Caloric goal of 1200 to 1800 kcal per day with 30% of calories from fat and > 15% from protein
  - At least 175 minutes of moderate-intensity physical activity per week
- Group and individual counseling sessions occurred weekly for the first 6 months
  - Months 7-12: 2 group, 1 individual session per month
  - Years 2-4: individualized basis with one in-person contact per month and an additional monthly email or phone call
  - After year 4, one individual contact a month and offered 2-3 group classes each year to help maintain interest and goals

Diabetes education and support
- Three group sessions per year that focused on diet, exercise, and social support for years 1 to 4
- In following years, one session was held per year

Primary Outcome:

Death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, and hospitalization from angina with follow-up period of 13.5 years

Results:

Primary outcome was not significant, as the outcome occurred in 403 patients in the intervention group and 418 patients in the control group (**p = 0.51**)

Patients in the intervention group had significant decreases in weight, waist circumference and A1C, as well as improved physical fitness

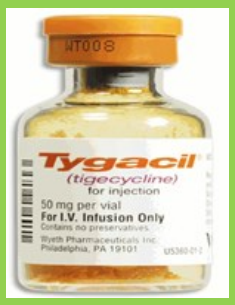
Severe hypoglycemia, gallstones, fractures, amputations, and congestive heart failure were monitored and were not significantly different between the two groups

Conclusions: Intensive lifestyle modifications did not reduce cardiovascular outcomes as compared to diabetes education and support. However, there was also no harm to intensive lifestyle modifications. This intervention did show positive effects on overall weight, physical fitness levels, waist circumference, and A1C levels. In addition, patients also experienced less urinary incontinence, sleep apnea, and depression, and improvements in quality of life, physical functioning, and mobility. Healthcare practitioners tend to recommend low carbohydrate, low fat, or Mediterranean diets instead of caloric intake restriction, such as 1800 calories per day. Therefore, observing those long-term benefits would be more beneficial and applicable. At this point in time, lifestyle modifications should continue to be recommended to patients.

FDA MedWatch Updates
September - December 2013

Prescribing and Dispensing Restrictions Loosened on Rosiglitazone

In 2010, the FDA placed prescribing and dispensing restrictions on Avandia® (rosiglitazone) due to data analysis that indicated rosiglitazone increased risk of myocardial infarctions in type 2 diabetic patients. This resulted in the FDA requiring placement of rosiglitazone in a Risk Evaluation and Mitigation Strategy (REMS) program, limiting the use of rosiglitazone and rosiglitazone-containing medications. But with recent re-evaluation of data from the Rosiglitazone Evaluated for Cardiovascular Outcomes and Regulation of Glycemia in Diabetes (RECORD) trial, the FDA announced that it will modify REMS program requirements, along with updated revisions to prescribing documentation and patient Medication Guides. Now, the FDA is no longer requiring patients, health care professionals and pharmacies to enroll in the rosiglitazone REMS program for the prescribing, dispensing or reception of rosiglitazone medications.



New Black Box Warning for Tigecycline

In September of 2013, the FDA notified the medical community of a new Black Box Warning for increased risk of death when intravenous Tygacil® (tigecycline) is used for both FDA-approved and non-FDA-approved uses. An evaluation of clinical trials in which tigecycline was used for FDA-approved indications (complicated skin and skin structure infections, complicated intra-abdominal infections, and community-acquired bacterial pneumonia) showed that the adjusted mortality rate for tigecycline was 2.5%, compared to 1.8% for other antimicrobial medications. The adjusted risk difference for death was 0.6% (95% Confidence Interval of 0.0, 1.2). The cause of mortality has not been established. The FDA recommends the reservation of tigecycline for use in situations in which alternative treatments are not available.

New Information Regarding Ponatinib and Blood Clot Risk

On December 20, 2013, the FDA issued an update requiring new safety measures for Iclusig® (ponatinib) to address the risk of life-threatening blood clots and severe narrowing of blood vessels. Earlier this year, the FDA started investigating an increased frequency of reports of blood clots and blood vessel narrowing in patients on the medication, resulting in Ariad Pharmaceuticals agreeing to suspend marketing and sales of the drug. The FDA provided instruction to health care providers whose patients had been benefitting from the drug on how to continue therapy. With the manufacturer addressing the concerns brought by the FDA, ponatinib has now returned to the U.S. market with an updated black box warning.

Ponatinib is FDA-approved for treatment of adults with chronic phase, accelerated phase or blast phase chronic myeloid leukemia (CML) or Philadelphia chromosome-positive acute lymphoblastic leukemia (ALL) who were no longer benefitting from, or tolerating, other treatment.

VA National Formulary Update:
Glyburide has been removed from the formulary. The medication is still orderable in CPRS but will soon be deactivated.

New Generics (Nov. 2013 - Jan. 2014)

Aciphex - Rabeprazole

Cymbalta - Duloxetine

Epivir - Lamivudine

Micardis - Telmisartan

Rapamune - Sirolimus

Twynsta - Amlodipine/ telmisartan

Brands Going Generic (Anticipated) Jan. 2014 - Jun. 2014

Actonel - Risedronate

Asacol - Mesalamine DR

Celebrex - Celecoxib

Evista - Raloxifene

Lunesta - Eszopiclone

Nexium - Esomeprazole

Renagel - Sevelamer

Tazorac gel - Tazarotene

Trillipix - Fenofibric acid

Viracept - Nelfinavir

Xeloda - Capecitabine

Continued from Page 2, Drug Information Corner

offenders.

TABLE 2: **SSRI & SNRI Half-life**

CLASS	DRUG	HALF-LIFE (hrs)
SSRI	Fluoxetine	84-144
	Paroxetine	21
	Sertraline	26
	Citalopram	35
	Escitalopram	27-32
SNRI	Venlafaxine	3-13
	Duloxetine	11-16

Managing and being familiar with the side effects of common psychoactive medications can be helpful when determining a patient's primary diagnosis or monitoring treatment response. Many antidepressants can cause anticholinergic effects including blurry vision, urinary hesitancy, abdominal cramps, dry mouth and constipation. The QTc prolonging effects of many psychoactive medications can be a crucial variable in deciding therapy for the patient's admission diagnosis, especially antimicrobial selection. Other frequent side effects include dizziness, sedation, weight gain and syndrome of inappropriate antidiuretic hormone (SIADH).[5] Although many of these effects are not life threatening, they can lead to reduced cognition and quality of life, making patient interaction more difficult.

Understanding the inpatient management and the consequences of discontinuing, initiating or continuing psychiatric medications may not only help maintain the stability of the patient's psychiatric disorder, but will also improve treatment outcomes. Being cautious and aware in the treatment of any patient on psychoactive medications is necessary to achieve optimum safety and outcomes.

References:
1) National Alliance on Mental Illness. Mental Illness and Veterans. https://www.nami.org/Template.cfm?Section=Mental_Illnesses1&Template=/TaggedPage/TaggedPageDisplay
2) Ward M, Schwartz A. Challenges in pharmacologic management of the hospitalized patient with psychiatric comorbidity.. J Hosp Med. 2013; 8(9): 523-9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/?term=challenges+in+pharmacologic+managemnet+of+the+hospitalized+patient+with+psych
3) Drug Tapering. Pharmacist's Letter 2008. Available from: http://pharmacistsletter.therapeuticresearch.com/pl/ArticleDD.aspx?nidchk=1&cs=PLPTLPHONLY~CEPDA&s=PL&pt=6&fpt=31&dd=241208&pb=PL&searchid=44193946
4) McAuley DF. Antidepressants (Adult dosing). GlobalRPh Inc. Last revised: 07/21/13; http://www.globalrph.com/antidepressants.htm
5) Jensen B, Regier L. Antidepressant Comparison Chart. Last revised: April 2013: www.rxfiles.ca

Tech Timeout: Alonzo

Alonzo Jones
Certified Pharmacy Technician
AFGE Local 1966 Vice President

Alonzo has spent over 10 years within the VA system. He started off in EMS, a department in which he served for a year and a half. He then entered the Upward Mobility program in order to receive formal training to become a pharmacy technician. Since completing the 2 year program and becoming a certified technician, he has spent his working days providing service to the inpatient side of the hospital.

While his day job involves patient safety and navigating the halls of the Lebanon VAMC, Alonzo has another passion- football. But Alonzo does not throw on cleats and run wind sprints. Alonzo prefers to run the show from the sidelines.

Over the last decade, he has been an owner of three semi-professional teams. Two teams, the Tigers and Silver Bullets, were located in York.

Then, in 2008, he organized and coached the Lebanon Valley Cardinals, a member of the Independent Football League (IFL). Over the course of 2 seasons, the Cardinals faced off against competition from Philadelphia, Delaware, Maryland and Washington, DC. According to Alonzo, the highlight of his time owning the Cardinals was when teams in the IFL were invited to play each other in the Wells Fargo Center- the home of the Philadelphia Soul of the Arena Football League.

Alonzo now spends his time coaching the ponies division for the Lebanon Friendship Chiefs. But a return to team ownership is in the works as the possibility exists for a semi-professional arena league team starting in the Lebanon area.

Pop Culture Pharmacy

1.) Which of the following is NOT a real movie?
A.) The Pharmacist
B.) Don't Shoot the Pharmacist!
C.) Your Friendly Neighborhood Pharmacist

2.) T/F: John Wayne once portrayed a pharmacist on film.
A.) True
B.) False

3.) Which of the following movies does NOT feature a pharmacist?
A.) It's a Wonderful Life
B.) Bill & Ted's Excellent Adventure
C.) Tyler Perry's Temptation

4.) What is the name of the pharmacist character on *Family Guy?*
A.) John
B.) Mort
C.) Joe
D.) Cleveland

5.) Which comedian joked: "Can you give me an explanation as to why the pharmacist has to be two-and-a-half feet up above everybody else?...Brain surgeons, airline pilots, nuclear physicists, we're all on the same level. Oh no, he's gotta be two-and-a-half feet up. 'Look out, everybody, I'm working with pills. Spread out, give me some room.' "?
A.) Jerry Seinfeld
B.) Larry David
C.) George Carlin
D.) Louis CK

6.) Match Game: Match the fictitious drug to the movie in which it appears:

A.) Misery (1990)	a.) Novril
B.) Side Effects (2013)	b.) Prozium
C.) Children of Men (2006)	c.) Ablixa
D.) Equilibrium (2002)	d.) Quietus

7.) Which of the following is an actual musical group?
A.) Over the Counter
B.) Rx for My Heart
C.) The Pill Counters
D.) Ted Leo and the Pharmacists

Answers on Page 7

LEBANON VAMC PHARMACY

Pop Culture Pharmacy Answers

1.) C
2.) A (bonus: The Duke's father, Clyde Morrison, was a pharmacist by trade)
3.) B
4.) B
5.) A
6.) A - a
B - c
C - d
D - b
7.) D

Continued From Page 1, New Drug Alert

new medications that will find their way into the treatment algorithm for COPD. One was for BREO ELLIPTA, a combination inhalation product containing fluticasone and vilanterol.[4] Breo Ellipta resembles other current therapies on the market, such as Advair® and Symibort®, in that it is a combination product featuring a corticosteroid and beta$_2$-agonist. Vilanterol, the beta$_2$-agonist component, is not approved in the U.S. as monotherapy.

Then, another drug received FDA approval right before the end of the year. On December 18, 2013, the FDA announced the approval of ANORO ELLIPTA for maintenance treatment of airflow obstruction in patients with COPD.[5] Like Breo Ellipta, Anoro Ellipta is a combination product that contains vilanterol, but in combination with umeclidinium, a long-acting anticholinergic agent. Combivent® Respimat® is a similar product but requires dosing four times a day. Anoro Ellipta is dosed one inhalation, once a day via a multidose, metered dry powder inhaler (DPI), at an FDA-approved strength of umeclidinium/vilanterol 62.5 mcg/25 mcg.[6]

Efficacy of Anoro Ellipta was shown in a dose-ranging trial that incorporated 1,908 patients with COPD or asthma and confirmatory trials that included two 6-month placebo-controlled trials, two 6-month active-controlled trials and two 12-week crossover trials in patients with COPD. In the 6 month trials, 4,733 patients with a diagnosis of COPD were enrolled with the following inclusion criteria: above the age of 40 years, post-albuterol $FEV_1 \leq 70\%$ of predicted normal values, FEV_1/FVC of < 0.7 and a Modified Medical Research Council (mMRC) score of ≥ 2. The primary endpoint was change from baseline in trough FEV_1 at Day 169. Umeclidinium/vilanterol 62.5 mcg/25 mcg showed a greater increase in change from baseline in trough FEV_1 versus placebo.[6]

Anoro Ellipta carries similar side effect warnings and precautions to other long-acting beta$_2$-agoninsts and anticholinergics. Common side effects include pharyngitis, sinusitis, lower respiratory tract infections, constipation, diarrhea, muscle spasms, neck pain and chest pain. Caution is advised in patients with cardiovascular disorders, glaucoma, BPH and diabetes. As with all medications containing a long-acting beta$_2$-agonist, Anoro Ellipta carries a Black Box Warning of an increased risk of asthma-related deaths.[6] The manufacturer is anticipating a release date in the first quarter of 2014.[5] Pricing for this product is currently unavailable.

References:

1) American Lung Association. Chronic Obstructive Pulmonary Disease (COPD) Fact Sheet. ADA. 2013. Available from: http://www.lung.org/lung-disease/copd/resources/facts-figures/COPD-Fact-Sheet.html.
2) Yale New Haven Services Corporation Center for Outcomes Research and Evaluation. Medicare Hospital Quality Chartbook: Performance Report on Outcome Comes. CMS. 2013. Available from: http://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/HospitalQualityInits/Downloads/-Medicare-Hospital-Quality-Chartbook-2013.pdf.
3) Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease (2013). Available from: http:/www.goldcopd.org/uploads/users/files/GOLD_Report_2013_Feb20.pdf.
4) BREO ELLIPTA (package insert). Research Triangle Park, NC. GlaxoSmithKline; 2013.
5) "ANORO ELLIPTA approved as first once-daily dual bronchodilator for the treatment of COPD in the US." *GSK*. 18 December 2013. Available from: http://us.gsk.com/html/media-news/pressreleases/2013/anoro_-ellipta_-approved-as-first-once-daily-dual-bronchodilator.html.
6) ANORO ELLIPTA (package insert). Research Triangle Park, NC. GlaxoSmithKline; 2013.